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Suture Formation, Premature Sutural Fusion, and Suture Default Zones in Apert Syndrome

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On the basis of our studies, we postulate that suture formation in Apert syndrome is related to the relative maturity of abutting calvarial bones. The fused coronal suture, a consistent manifestation at birth, develops first because the ossification centers of the frontal and parietal bones are in intimate contact early during intrauterine life. Calvarial immaturity and the megalencephalic brain characteristic of the Apert syndrome appear to work in concert to produce a widely patent midline calvarial defect extending from the glabella to the posterior fontanelle. Because sagittal growth in the coronal sutures cannot take place, the megalencephalic brain grows upward and laterally, and bulges forward through the midline defect. The defect fills in by coalescence of bony islands without proper suture formation because the gap to be bridged is so great that the time window for developing sutural interdigitations may have closed. Other sutures, such as the lambdoid, squamosal, and sphenotemporal, develop with normal interdigitations because abutting bone margins are in close enough proximity to permit suture formation.

KEY WORDS: acrocephalosyndactyly, sutures, suture formation, suture default zones, craniosynostosis

INTRODUCTION

In our previous studies of the infant Apert calvaria [Kreiborg and Cohen, 1990; Kreiborg et al., 1993], we observed: 1) congenitally fused coronal sutures; 2) a widely patent midline calvarial defect extending from the glabella to the posterior fontanelle; and 3) normal appearance of other calvarial sutures. We suggested that the midline defect represented a *suture default zone*[1] because no proper interdigitated suture formation takes place. Rather, the midline defect is obliterated during the first few years of life by coalescence of bony islands that form in the defect (Figs. 1A,C, 2). The term craniosynostosis appears to be misleading when applied to the metopic and sagittal regions in Apert syndrome because no sutures form ab initio that then become prematurely fused.

In this paper, we set forth our ideas about suture formation, premature sutural fusion, and suture default zones, all of which occur in Apert syndrome. By studying a 1-year-old Apert skull from the Greig collection at the Royal College of Surgeons in Edinburgh, together with more recent observations on two Apert infant skulls from the Pathological Museum of the University of Leiden and our earlier work with radiographs and three-dimensional CT reconstructions [Kreiborg and Cohen, 1990; Kreiborg et al., 1993], we attempt to explain the seemingly paradoxical phenomena of premature sutural fusion and suture default zones concurring in the same disorder.

NORMAL SUTURE FORMATION

A normal cranial suture is a fibrous articulation that permits enlargement of the brain. Thus, sutures prevent adjacent bones from coalescing [Cohen, 1993]. Normal closure of the metopic suture[2] begins at the level of the frontal eminences and proceeds superiorly to the

[1]We now prefer the term *suture default zone*, rather than our earlier *suture area* [Kreiborg and Cohen, 1990], to designate the midline defect which lacks proper suture formation. The term *suture area* suggests a region where suture formation takes place. Also, Moss [1957, 1958] defined a *suture area* as adjacent edges of bone together with the soft tissue that separates them, and a *suture proper* as the soft-tissue component only.

[2]Usually obliterated by the third year; persists throughout life in 10%.

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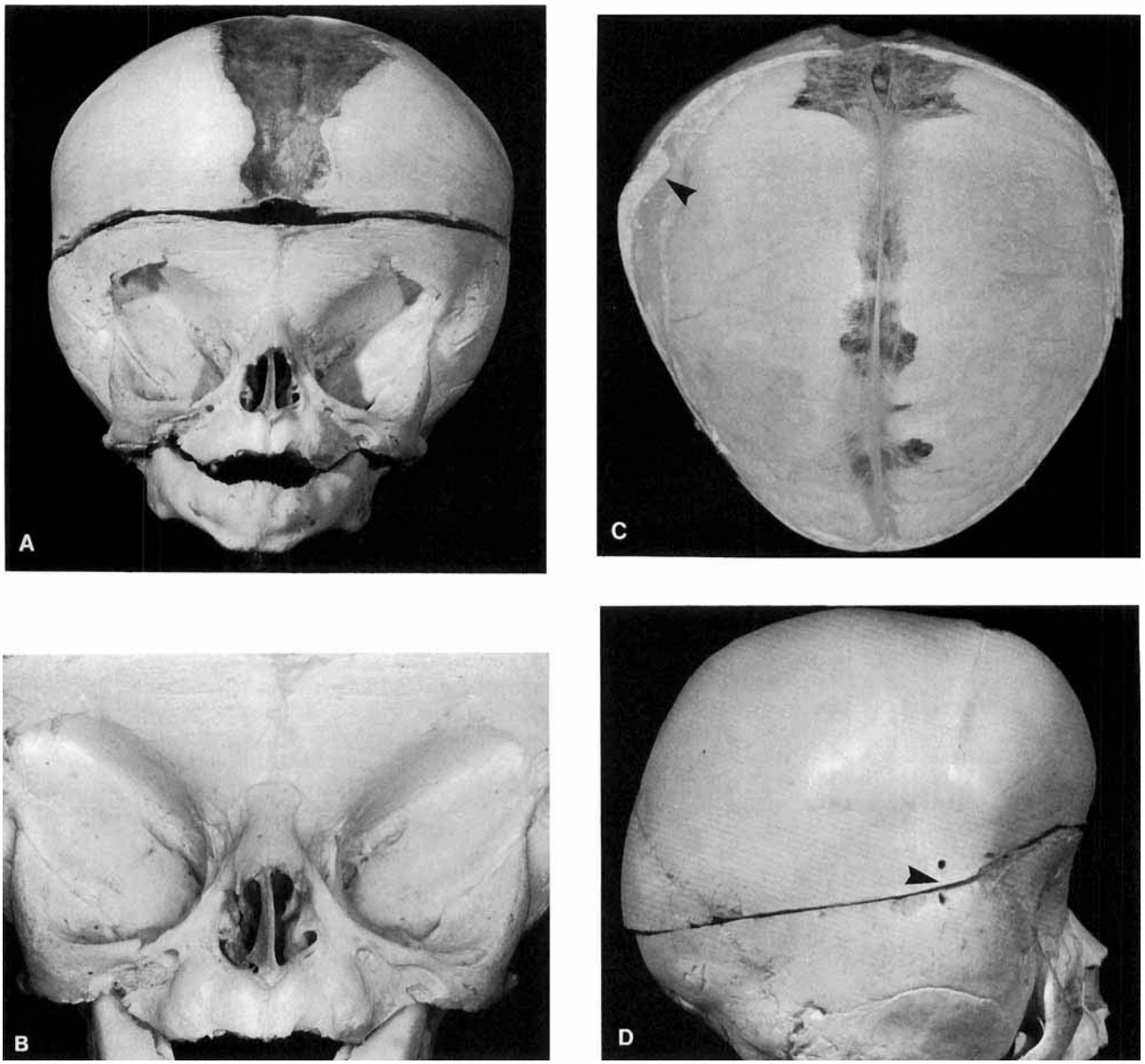

Fig. 1. Apert skull (1-year-old boy). From the Greig Collection, Royal College of Surgeons, Edinburgh. **A:** Note wide calvarial midline defect. **B:** Close-up of fronto-orbital region, showing intact supranasal portion of the frontal suture. **C:** Internal view of hypoplastic, paper-thin calvaria. Note irregular closure of midline defect with persistence of large gaps. Also note thickening of bone, representing initial fusion of ossification centers of frontal and parietal bones (arrow). **D:** Note closed coronal region associated with posteriorly convex curvature. All other sutures are patent. Note interdigitated lambdoid suture with associated Wormian bone. Also note fusion of ossification centers of frontal and parietal bones (arrow).

bregma. A small supranasal portion of the metopic suture remains unobliterated until the sixth year of life, although remnants of the suture may persist into adult life. All other cranial sutures normally do not fuse until adult life. Coronal sutures normally begin fusing inferiorly and proceed superiorly to the bregma.[3]

[3]Isolated, nonsyndromic coronal synostosis is known to begin inferiorly and gradually extend superiorly [Albright and Byrd, 1982].

APERT SYNDROME

Coronal Fusion

The coronal sutures are invariably closed at birth, and an osseous condensation line is observed radiographically (Fig. 3), by CT scan, and on the skull (Fig. 1D). On the inner table, bone indentations are seen along the suture. On the outer table, the fused suture is characterized by bone thickening. The small squama of the frontal bone and the backward convex outline of the fused coronal suture suggest that closure takes place

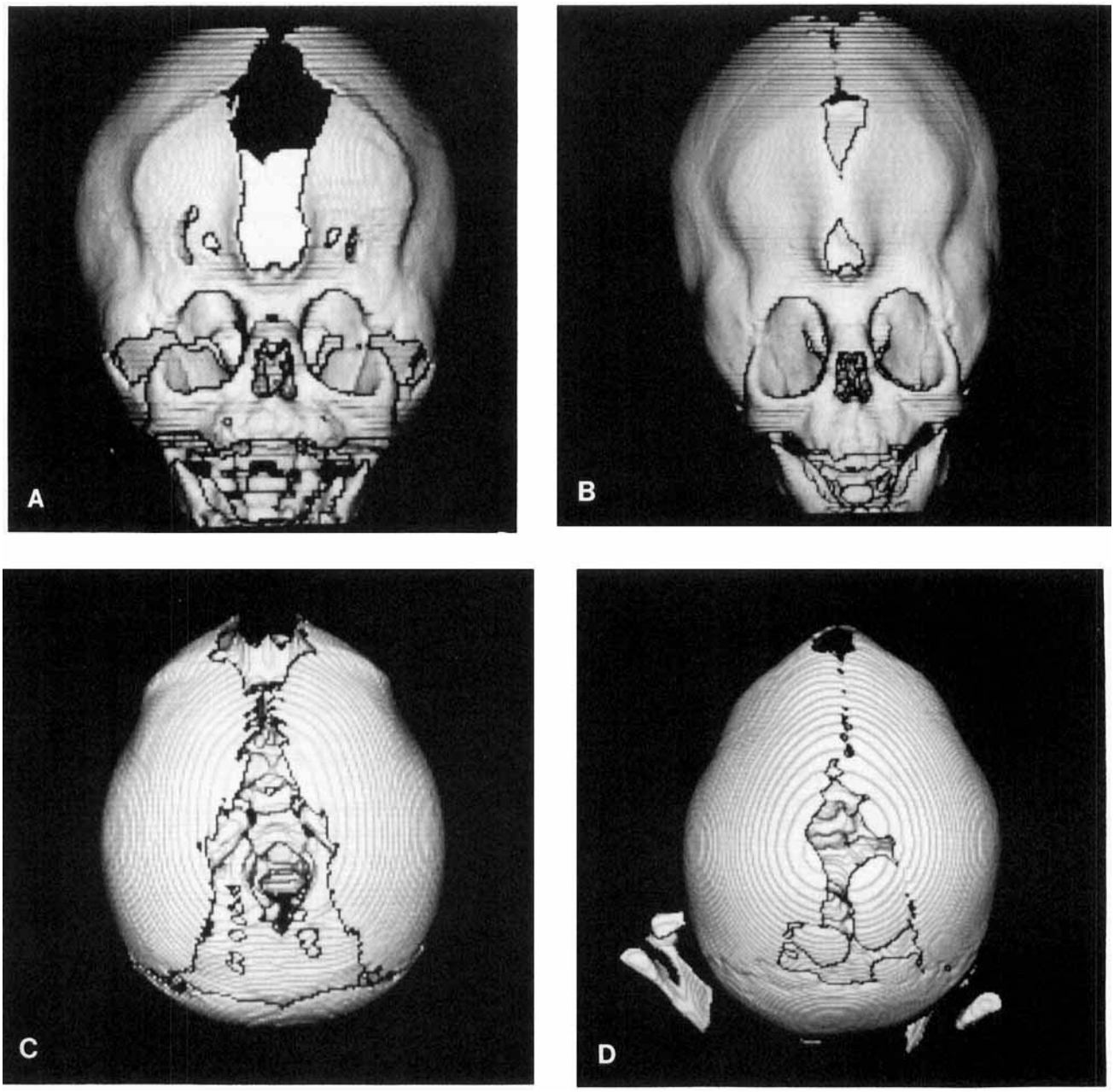

Fig. 2. Three-dimensional reconstruction of CT scans in an Apert infant. **A:** Extensive midline calvarial defect and unusually large anterolateral fontanelles extending into orbits at age 1 month. **B:** Note ongoing closure of midline calvarial defect and closure of anterolateral fontanelles in same patient at age 8 months. **C:** Calvarial view showing widely patent midline defect at age 1 month. **D:** Calvarial view of same patient at age 8 months, showing ongoing closure of midline defect with coalescence of bony islands; no proper suture formation.

very early during intrauterine life [Kreiborg et al., 1993] (Figs. 1D, 3). Synostosis has an inferior-superior gradient, but is incomplete at its most superior end, which remains an inactive open fissure because no displacement takes place between the frontal and parietal bones (Figs. 3, 4). The fissure gradually undergoes bony obliteration.

The lateral and caudal displacement of the ossification center of the frontal bone leads to horizontal orientation of the ossification lines of the squama frontalis (Fig. 1A). It is conceivable that the more vertical ossification of the zygomatic process of the frontal bone is thereby delayed (Fig. 2A).

Metopic and Sagittal Default Zones

The metopic and sagittal sutures are discussed together because the midline defect affects both. In the infant Apert skull less than age 3 months, a wide midline calvarial defect extends about 1.5 cm above the nasofrontal suture (nasion) through the sagittal gap be-

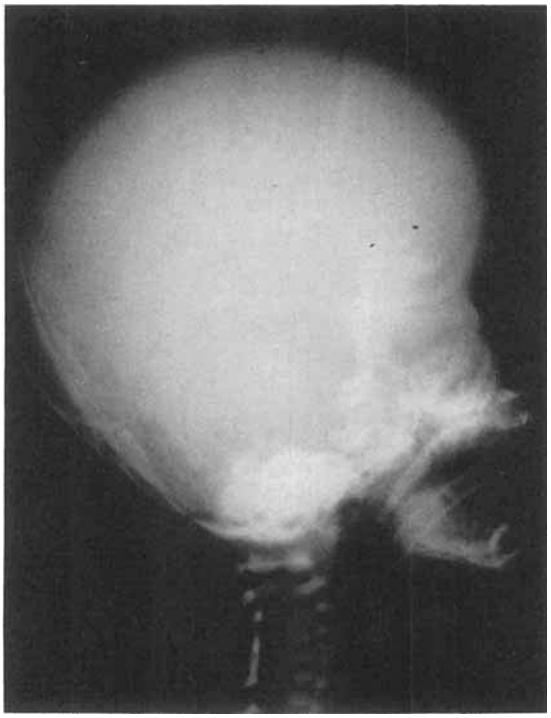

Fig. 3. Radiograph of Apert newborn (at 31 weeks of gestation), showing coronal fusion with patent fissure superiorly.

tween the two frontal and the two parietal bones to the posterior fontanelle. The defect widens toward the anterior fontanelle (Figs. 1A, 2A). The edges of the bony defect have bone spicules extending horizontally towards the midline. Just below the lower extent of the midline defect, a true metopic suture is found extending from the nasofrontal suture about 1.5 cm superiorly (Fig. 1B). The sagittal suture zone shows the same midline defect (Figs. 1C, 2C) and is continuous with that observed in the metopic zone. The edges of the parietal bones are irregular (Figs. 1C, 2C), with bony spicules extending medially.

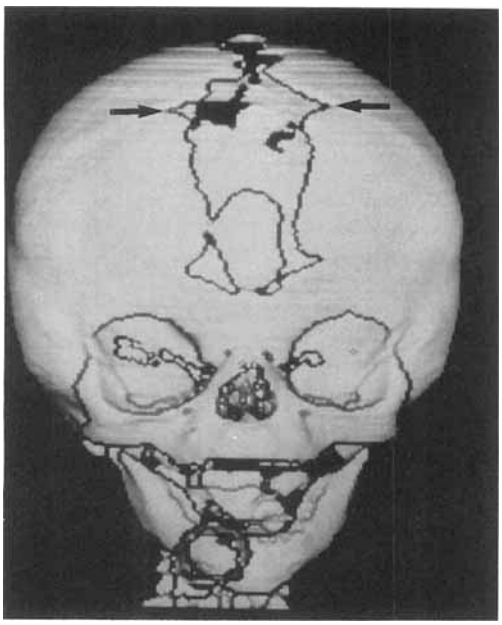

Fig. 4. Three-dimensional reconstruction of CT scan showing bony island developing in midline calvarial defect. Note angular areas (arrows) representing patent coronal suture fissures superiorly.

In the midline defect from the glabella to the posterior fontanelle, islands of bone begin to form and gradually coalesce (Figs. 2B,D, 4). They can begin anywhere in the midline defect, and coalescence ultimately leads to bony obliteration during the first few years of life (Fig. 2B,D). Bony islands forming in the midline defect are *not* Wormian bones because they never develop the interdigitations of true Wormian bones, but simply coalesce with each other and with the calvarial bones to obliterate the midline gap.[4]

Cohen [1993] indicated that in isolated sagittal or metopic synostosis, pronounced sutural ridging was a common occurrence. However, this does not occur in Apert syndrome because of the midline calvarial defect, its lack of proper suture formation with interdigitations, and its closure by coalescence of bony islands. The midline defect in the metopic zone can sometimes appear as a midfrontal "bulge" (Fig. 5). This has erroneously been called metopic synostosis with "median vertical frontal gibbosity" [Marsh et al., 1991] or frontal encephalocele (Fig. 6) when, in fact, it is neither (Fig. 7).

Lambdoid Suture

The lambdoid suture shows the true interdigitations of a normal suture. Furthermore, Wormian bones, which occur most commonly in the normal lambdoid suture, were found in two of our Apert cases. They were true Wormian bones with interdigitations that articulated with the parietal and occipital bones (Fig. 1D).

Squamosal and Sphenotemporal Sutures

Dry skull study shows that squamosal and sphenotemporal sutures with interdigitations are also evident (Fig. 1D). Thus, true suture formation also characterizes these calvarial articulations.

DISCUSSION

We postulate that suture formation in Apert syndrome is related to the relative maturity of abutting calvarial bones. In every instance, abutting bones are in close enough proximity for suture formation to take place except in the midline. The fused coronal suture develops first because the ossification centers of the frontal and parietal bones are in intimate contact with each other very early during intrauterine life. The infant calvaria is hypoplastic and paper-thin (Fig. 1C). Calvarial immaturity[5] and the megalencephalic brain

[4]Park and Powers [1920] called these Wormian bones. However, because longitudinal radiographs and three-dimensional reconstructions of CT scans were not available at that time, it was an understandable historical error for these great observers to

[5]Besides the hypoplastic, paper-thin calvaria, other signs of skull immaturity include large anterolateral fontanelles that extend into the orbits (Fig. 2A) and patent posterolateral fontanelles.

Fig. 5. Midline calvarial defect may result in a pseudoencephalic appearance of forehead. Infant male, age 2½ weeks (CCFA #984, courtesy of S. Pruzansky, Center for Craniofacial Anomalies, Chicago, IL.

characteristic of Apert syndrome [Cohen and Kreiborg, 1990, 1993, 1994] appear to work in concert to produce the midline defect. Because sagittal growth in the coronal sutures cannot take place, the megalencephalic brain grows upward and laterally and bulges forward through the midline defect. Since expansion in the width of the cranial base is relatively limited, the two sides of the frontal bones do meet inferiorly to form a metopic suture extending from the nasofrontal suture about 1.5 cm superiorly to the beginning of the midline defect.

Fig. 6. Lateral cephalogram of Apert infant, showing midline defect with exposed brain, simulating encephalocele. This is not a true encephalocele, however, because midline defect will eventually be completely covered with bone.

Fig. 7. Same patient as in Figure 5, but at age 10 years. Note bone has completely covered defect in forehead. *No surgical procedures were carried out on the frontal bone* (CCFA #984, courtesy of S. Pruzansky, Center for Craniofacial Anomalies, Chicago, IL).

The midline defect fills in by coalescence of bony islands without proper suture formation because the gap to be bridged is so great that the time window for developing interdigitations may have closed. Other sutures, such as the lambdoid, squamosal, and sphenotemporal, develop properly with normal interdigitations because abutting bone margins are in close enough proximity to permit proper suture formation (Table I).

CONCLUSIONS

Our analysis of suture formation, premature sutural fusion, and suture default zones in Apert syndrome is based on skull radiographs, longitudinal cephalometric radiographs, three-dimensional reconstructions of CT scans, dry skulls, and brain weights [Cohen and Kreiborg, 1990; Kreiborg et al., 1993; Cohen and Kreiborg, 1993, 1994]. To date, histologic studies of the craniofacial region have emphasized the cranial base [Kreiborg et al., 1976; Stewart et al., 1977; Ousterhout and Melsen, 1982]. Histologic studies of calvarial sutures and suture default zones in Apert syndrome have not yet been carried out and are needed as opportunities arise at autopsy.

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TABLE I. Sutures and Suture Zones in Apert Syndrome

Region	Characteristics
Metopic below glabella	Suture formation
Metopic above glabella	Suture default zone; part of midline calvarial defect; closure by coalescence of bony islands
Sagittal	Suture default zone; part of midline calvarial defect; closure by coalescence of bony islands
Coronal	Suture formation; prematurely synostosed at birth
Lambdoid	Suture formation; true Wormian bones on occasion
Squamosal	Suture formation
Sphenotemporal	Suture formation

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